

Expanded Helicenes: A General Synthetic Strategy and Remarkable Supramolecular and Solid-State Behavior

Gavin R. Kiel,¹ Sajan C. Patel, Patrick W. Smith, Daniel S. Levine,¹ and T. Don Tilley*

Department of Chemistry, University of California, Berkeley, Berkeley, California 94720, United States

S Supporting Information

ABSTRACT: A divergent synthetic strategy allowed access to several members of a new class of helicenes, the “expanded helicenes”, which are composed of alternating linearly and angularly fused rings. The strategy is based on a three-fold, partially intermolecular $[2+2+n]$ ($n = 1$ or 2) cycloaddition with substrates containing three diyne units. Investigation of aggregation behavior, both in solution and in the solid state, revealed that one of these compounds forms an unusual homochiral, π -stacked dimer via an equilibrium that is slow on the NMR time scale. The versatility of the method was harnessed to access a selenophene-annulated expanded helicene that, in contrast to its benzannulated analogue, exhibits long-range π -stacking in the solid state. The new helicenes possess low racemization barriers, as demonstrated by dynamic ^1H NMR spectroscopy.

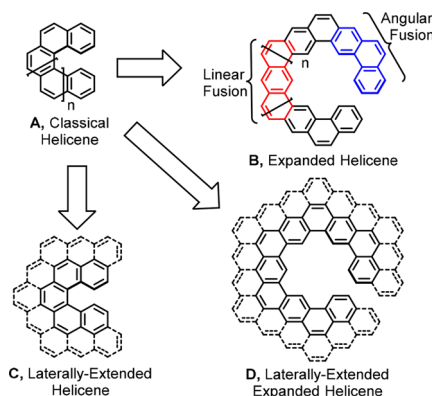


Figure 1. Simple classification of larger helicenes.

A helicene has been defined as “a polycyclic aromatic hydrocarbon (PAH) with a nonplanar, screw-shaped skeleton formed by ortho-fused benzene or other aromatic rings”.¹ These compounds display remarkable properties^{1d} such as large nonlinear optical responses,² circularly polarized absorption and emission,³ rich supramolecular chemistry,⁴ and relatively high solubility. Thus, helicenes are now being investigated for applications in electronics and optoelectronics,^{3b,c,5} asymmetric catalysis (e.g., as ligands),⁶ molecular recognition,⁷ and as molecular machines and switches.⁸ Due to their significant distortion from planarity and resulting three-dimensional structure, helicenes also offer the possibility of novel intermolecular interactions in the solid state (e.g., π -stacking in two or three dimensions).⁹ Toward this end, helicenes play an important role in the growing field of crystal engineering with nonplanar PAHs.¹⁰

Most reported helicenes possess all angularly fused aromatic rings (A, Figure 1). Increasing the size of a helicene by alternation of linear and angular ring fusion (“expanded helicene”, B) or lateral extension of its π -system (“laterally extended helicene”, C) might result in novel electronic, photophysical, and chiroptical properties. The possible increase in π -stacking could result in discovery of new or enhanced supramolecular or solid-state properties (e.g., higher charge-carrier mobilities). Their flexible structures should make them more soluble than analogous linear PAHs and their larger cavities are conducive to applications that rely on porosity (e.g., sensing or catalysis).

A growing number of laterally extended helicenes have been well-characterized,¹¹ but expanded helicenes are unexplored. The term “expanded heterohelicene” was used to describe a helicene-like compound with alternating angular and linear fusion of six-membered rings; however, this compound contains several saturated rings.¹² A few other helical PAHs with expanded cavities are known. For example, Vollhardt reported a series of heliphenes, which are composed of alternating six- and four-membered rings fused in an angular fashion.¹³

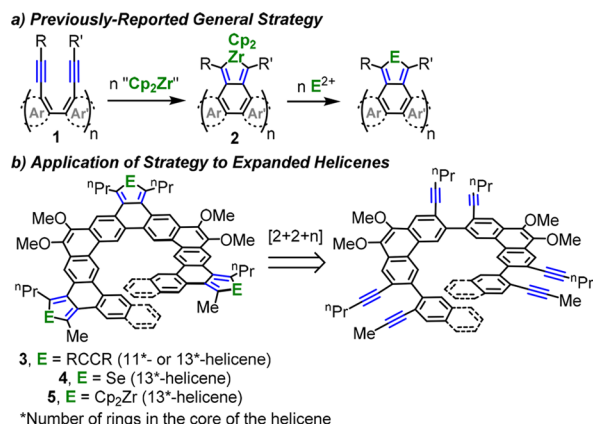
The central challenge associated with the investigation of helicenes is their difficult synthesis, which requires both the introduction of strain and regioselective fusion of many rings. Many methods have been developed,^{1b} including photocyclization of stilbenes,¹⁴ Diels–Alder cycloaddition,¹⁵ and fully intramolecular $[2+2+2]$ cycloisomerization.^{13,16} These methods have allowed exhaustive studies of classical helicenes, but they are difficult to apply to expanded helicenes, for which the central challenge is regioselective fusion of many rings.

As part of an effort to increase the utility of $[2+2+n]$ cycloadditions in PAH synthesis, we recently developed a strategy for the synthesis of large PAHs via zirconocene coupling, involving the reductive cyclization of oligo(diynes) (1, Scheme 1a) to form zirconacyclopentadiene-annulated PAHs (2).¹⁷ Two compelling features of this strategy are the near-quantitative nature of the zirconocene coupling reaction and the known synthetic versatility¹⁸ of the resulting zirconacyclopentadiene functionality.

Received: October 17, 2017

Published: December 7, 2017

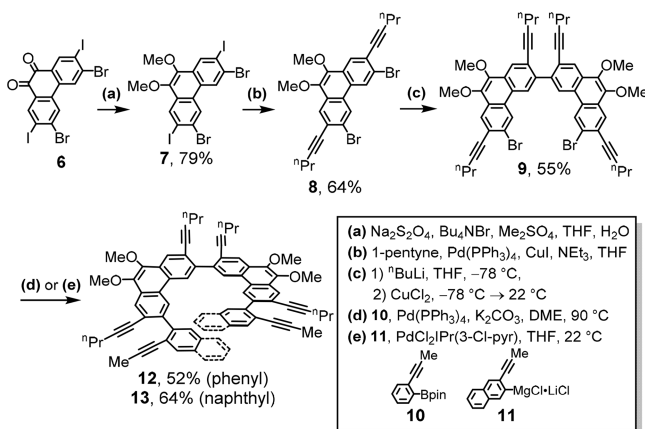
Scheme 1



Here we report a general strategy for use of $[2+2+n]$ cycloadditions in the synthesis of expanded helicenes (Scheme 1b). The effort was aided by identification of a *catalytic* and essentially *quantitative* $[2+2+2]$ cycloaddition to access a series of benzannulated expanded helicenes (3). This partially intermolecular $[2+2+2]$ reaction was enabled by a commercially available Ir catalyst and is complementary to the stoichiometric zirconocene-coupling reaction used to access expanded helicenes 4 and 5. One of the benzannulated expanded helicenes undergoes an unusual, diastereoselective dimerization via π -stacking, both in solution and in the solid state, while a quite different solid-state packing was observed for analogous 4. Finally, the presence of diastereotopic Cp rings in 5 allowed the determination of its racemization barrier by dynamic ^1H NMR spectroscopy, suggesting that expanded helicenes are much more flexible than all-angularly fused helicenes.

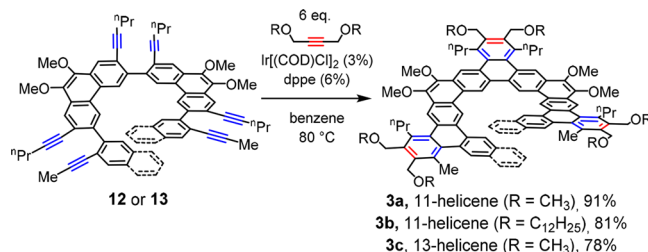
Execution of the synthetic strategy was enabled by the availability of 6 (Scheme 2) in large (>100 g) quantities.²⁰ This

Scheme 2. Synthesis of Expanded Helicene Precursors



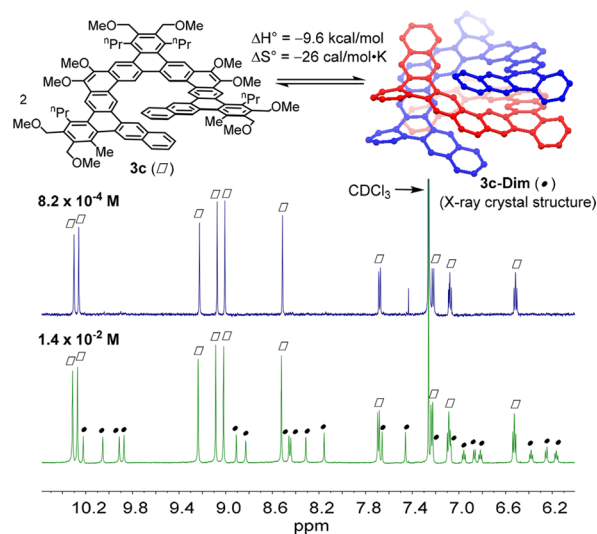
compound was reduced and methylated in one pot to give 7 using a scalable protocol for a similar compound,²¹ and a subsequent Sonogashira reaction²² gave diyne 8. A selective monolithiation of 8 with $^n\text{BuLi}$ permitted a CuCl_2 -mediated oxidative homocoupling to give tetrayne 9. Finally, cross-coupling of 9 with metalated (alkynyl)benzene 10 and (alkynyl)naphthalene 11 gave tris(diyne)s 12 and 13 in 52 and 64% yields, respectively.

An optimal $[2+2+2]$ catalytic system was identified for the ring-fusion reaction (Scheme 3), based on modification of a

Scheme 3. Expanded Helicenes via a Three-Fold, Partially Intermolecular, Ir-Catalyzed $[2+2+2]$ Cycloaddition

previously reported procedure²³ employing $[\text{Ir}(\text{COD})\text{Cl}]_2$ and dppe. Treatment of tris(diyne)s 12 and 13 with 6 equiv (2 equiv per diyne unit) of the corresponding monoyne in the presence of this catalyst produced the corresponding monoyne expanded 11-helicenes 3a,b and expanded 13-helicene 3c in good to excellent isolated yields. Helicenes 3a–c are very soluble in CH_2Cl_2 and THF (>100 mg/mL), which is notable given their size, and 3b is similarly soluble in hexanes. The remarkable efficiency of this reaction is indicated by ^1H NMR spectroscopy, which revealed essentially quantitative formation of 3a–c. This suggests its applicability to even larger expanded helicenes utilizing more than three couplings (including polymers).

A ^1H NMR analysis of a dilute (8.2×10^{-4} M) solution of 3c in chloroform-*d* is consistent with a monomeric expanded 13-helicene; however, concentration of this solution results in the emergence of a new species with reduced symmetry and upfield-shifted aromatic resonances (Scheme 4). The structure

Scheme 4. Slow Equilibrium between Expanded 13-Helicene and Its Homochiral, π -Stacked Dimer

of this new species was assigned via ^1H – ^1H NOESY (Figure S1) as the homochiral, π -stacked dimer 3c-Dim. The presence of a monomer–dimer equilibrium was confirmed by variable-concentration ^1H NMR spectroscopy (Figure S2). Variable-temperature ^1H NMR spectroscopy allowed measurement of thermodynamic parameters ($\Delta H^\circ = -9.6 \pm 0.3 \text{ kcal/mol}$ and $\Delta S^\circ = -26 \pm 1.0 \text{ cal/mol}\cdot\text{K}$) (Figures S3 and S4). The chemical shifts for 3c-Dim do not vary with concentration,

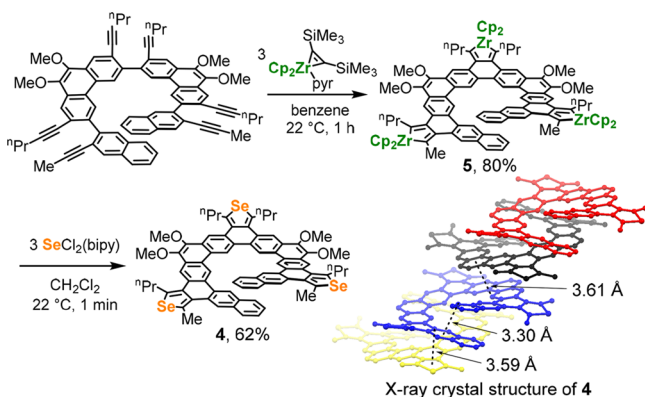
suggesting that there is no further aggregation (e.g., tetramers). This slow, unusual dimerization is likely driven by π -stacking between helicenes. Notably, PAH aggregation equilibria that are slow enough to be directly observed by ^1H NMR spectroscopy are extremely rare.²⁴

Single-crystal X-ray crystallography on **3c** revealed the same dimeric structure **3c-Dim** in the solid state, with the helicenes in the dimer related by a pseudo- C_2 axis of symmetry. The distorted nature of the helicene in its dimeric form can be quantified by its pitch of 7.44 Å, which was calculated by fitting a helical curve to the 13 centroids of the inner rings.²⁵ For comparison, the DFT-calculated structure of the monomer revealed a pitch of 3.30 Å (see SI). Due to the presence of the pseudo- C_2 axis in the dimer, half of the pitch of its monomeric component (3.72 Å) can be used as an estimate of the average π -stacking distance between the two helicenes. The true average π -stacking distance is shorter since this is formally the distance between centroids, which are not aligned. The chiral dimers co-crystallize with their dimeric enantiomer in the centrosymmetric space group $P2_1/c$. There are no π -stacking interactions *between* dimers, which is consistent with the observed solution behavior (*vide supra*), and large voids in the crystal are filled by chloroform-*d* (2.5 equiv per helicene).

In contrast to expanded 13-helicene **3c**, no aggregation is apparent in chloroform-*d* solution for the analogous 11-helicene **3a**, as ^1H chemical shifts are invariant over concentrations between 4.2×10^{-2} and 8.4×10^{-5} M (Figure S5). However, when the more soluble analogue **3b** is dissolved in methylcyclohexane-*d*₁₄ (at 22 °C), the ^1H NMR spectrum consists of a complex mixture of broadened and upfield-shifted resonances. Variable-temperature ^1H NMR spectroscopy (Figure S6) suggests this results from aggregation of some type.

While the dimerization of **3c** is interesting, extended π -stacking is often desirable (e.g., for applications that require efficient charge transport). Given that the presence of heteroatoms has a profound impact on self-assembly, selenophene-annulated expanded helicene **4** was targeted (Scheme 5). This compound was accessible in two steps

Scheme 5. Expanded Helicenes via Zirconocene Coupling

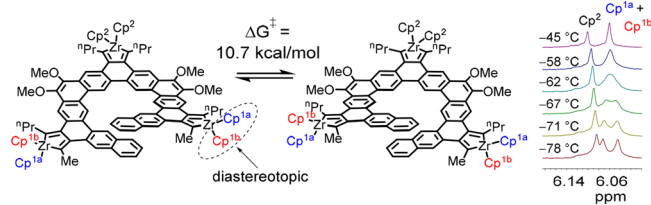


from tris(diyne) **13**, via the intermediacy of zirconacyclopentadiene-annulated expanded helicene **5**. In contrast to the analogous **3c**, compound **4** crystallizes with long-range π -stacking, as revealed by single-crystal X-ray diffraction. The helicenes stack as alternating *M* and *P* enantiomers, with a shortest intermolecular π - π distance of 3.6 Å. Helicene **4** exhibits a small pitch of 3.23 Å in the solid state, which is consistent with its DFT-calculated pitch of 3.29 Å. The small

itches for monomeric **3c** (calculated) and **4** (calculated and experimental) appear to be driven by a π -stacking interaction at their termini. These pitches are much smaller than those of topologically similar [7]helicene²⁶ and [7]heliophene,^{13a} which are 3.82 and 4.29 Å, respectively.

The new expanded helicenes possess low racemization barriers, which is evident in their room temperature ^1H NMR spectra. There are sharp singlets for the diastereotopic methylene resonances in compounds **3a**–**c** and only two Cp-H singlets (in 2:1 ratio) for **5**. Due to its monomeric nature and diastereotopic Cp rings, **5** provides an opportunity to study the configurational lability of the expanded 13-helicene framework by dynamic ^1H NMR spectroscopy (Scheme 6). Upon cooling

Scheme 6. Racemization Barrier in Expanded 13-Helicene



a toluene-*d*₈/tetrahydrofuran (3:1) solution of **5**, the more intense singlet decoalesces, giving a 1:1:1 singlet ratio. This allowed calculation of a racemization barrier ($\Delta G^\ddagger_{-62\text{ °C}}$) of 10.7 kcal/mol. The barriers for [7]helicene²⁷ and [7]heliophene^{13a} are 41.7 ($\Delta G^\ddagger_{27\text{ °C}}$) and 12.6 kcal/mol ($\Delta G^\ddagger_{-27\text{ °C}}$), respectively. The low barrier compared to [7]helicene might be attributed to the fact that the distortion required for racemization is spread over a larger number of bonds and angles (as for [7]heliophene).

In conclusion, five highly functionalized expanded helicenes were synthesized using a general, divergent strategy, which allowed studies on supramolecular organization and configurational stability. This generality will allow a systematic investigation of this fascinating compound class. We are currently exploring ways to increase configurational stability and reliably control supramolecular organization. Most importantly, the synthetic strategy should be applicable to other PAH topologies and graphene nanostructures.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b10902.

X-ray crystallographic data for **3c** (CIF)

X-ray crystallographic data for **4** (CIF)

Experimental procedures and characterization data for all new compounds, including Figures S1–S43 and Tables S1–S4 (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*tdtilley@berkeley.edu

ORCID

Gavin R. Kiel: 0000-0001-6449-8547

Daniel S. Levine: 0000-0001-8921-3659

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was funded by the National Science Foundation under Grant No. CHE-1708210. Crystallographic analysis was performed at The Advanced Light Source, which is supported by the Director, Office of Science, Office of Basic Energy Sciences, of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231. We thank Cynthia Hong for assistance with NMR spectroscopy and Stephen von Kugelgen for helpful discussions.

■ REFERENCES

- (1) (a) Shen, Y.; Chen, C.-F. *Chem. Rev.* **2012**, *112*, 1463. (b) Gingras, M. *Chem. Soc. Rev.* **2013**, *42*, 968. (c) Gingras, M.; Félix, G.; Peresutti, R. *Chem. Soc. Rev.* **2013**, *42*, 1007. (d) Gingras, M. *Chem. Soc. Rev.* **2013**, *42*, 1051. (e) Rickhaus, M.; Mayor, M.; Juriček, M. *Chem. Soc. Rev.* **2016**, *45*, 1542.
- (2) Verbiest, T.; Elshocht, S. V.; Kauranen, M.; Hellemans, L.; Snauwaert, J.; Nuckolls, C.; Katz, T. J.; Persoons, A. *Science* **1998**, *282*, 913.
- (3) (a) Field, J. E.; Muller, G.; Riehl, J. P.; Venkataraman, D. *J. Am. Chem. Soc.* **2003**, *125*, 11808. (b) Yang, Y.; Correa da Costa, R.; Fuchter, M. J.; Campbell, A. J. *Nat. Photonics* **2013**, *7*, 634. (c) Brandt, J. R.; Wang, X.; Yang, Y.; Campbell, A. J.; Fuchter, M. J. *J. Am. Chem. Soc.* **2016**, *138*, 9743.
- (4) (a) Nuckolls, C.; Katz, T. J.; Castellanos, L. *J. Am. Chem. Soc.* **1996**, *118*, 3767. (b) Shcherbina, M. A.; Zeng, X.; Tadjiev, T.; Ungar, G.; Eichhorn, S. H.; Phillips, K. E. S.; Katz, T. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 7837.
- (5) (a) Brandt, J. R.; Salerno, F.; Fuchter, M. J. *Nat. Rev. Chem.* **2017**, *1*, 45. (b) Yang, Y.; Rice, B.; Shi, X.; Brandt, J. R.; Correa da Costa, R.; Hedley, G. J.; Smilgies, D.-M.; Frost, J. M.; Samuel, I. D. W.; Otero-de-la-Rozza, A.; Johnson, E. R.; Jelfs, K. E.; Nelson, J.; Campbell, A. J.; Fuchter, M. J. *ACS Nano* **2017**, *11*, 8329. (c) Vacek, J.; Chocholoušová, J. V.; Stará, I. G.; Starý, I.; Dubí, Y. *Nanoscale* **2015**, *7*, 8793.
- (6) Narcis, M. J.; Takenaka, N. *Eur. J. Org. Chem.* **2014**, *2014*, 21.
- (7) Chen, C.-F.; Shen, Y. *Helicene Chemistry*; Springer: Berlin/Heidelberg, 2017; pp 201–220.
- (8) (a) Schweinfurth, D.; Zalibera, M.; Kathan, M.; Shen, C.; Mazzolini, M.; Trapp, N.; Crassous, J.; Gescheidt, G.; Diederich, F. *J. Am. Chem. Soc.* **2014**, *136*, 13045. (b) Shen, C.; Loas, G.; Srebro-Hooper, M.; Vanthuyne, N.; Toupet, L.; Cador, O.; Paul, F.; López Navarrete, J. T.; Ramírez, F. J.; Nieto-Ortega, B.; Casado, J.; Autschbach, J.; Vallet, M.; Crassous, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 8062.
- (9) (a) Ball, M.; Zhong, Y.; Wu, Y.; Schenck, C.; Ng, F.; Steigerwald, M.; Xiao, S.; Nuckolls, C. *Acc. Chem. Res.* **2015**, *48*, 267. (b) Fujikawa, T.; Segawa, Y.; Itami, K. *J. Am. Chem. Soc.* **2015**, *137*, 7763.
- (10) Gsänger, M.; Oh, J. H.; Könemann, M.; Höffken, H. W.; Krause, A.-M.; Bao, Z.; Würthner, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 740.
- (11) We include contorted aromatics and related compounds containing multiple helicenes embedded in a larger PAH framework. Examples with a single helical axis: (a) Schlütter, F.; Nishiuchi, T.; Enkelmann, V.; Müllen, K. *Angew. Chem., Int. Ed.* **2014**, *53*, 1538. (b) Schuster, N. J.; Paley, D. W.; Jockusch, S.; Ng, F.; Steigerwald, M. L.; Nuckolls, C. *Angew. Chem., Int. Ed.* **2016**, *55*, 13519. (c) Fujikawa, T.; Segawa, Y.; Itami, K. *J. Org. Chem.* **2017**, *82*, 7745. Examples with multiple helical axes: (d) Ref 9. (e) Barnett, L.; Ho, D. M.; Baldrige, K. K.; Pascal, R. A., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 727. (f) Wang, X.-Y.; Wang, X.-C.; Narita, A.; Wagner, M.; Cao, X.-Y.; Feng, X.; Müllen, K. *J. Am. Chem. Soc.* **2016**, *138*, 12783. (g) Fujikawa, T.; Segawa, Y.; Itami, K. *J. Am. Chem. Soc.* **2016**, *138*, 3587. (h) Pradhan, A.; Dechambenoit, P.; Bock, H.; Durola, F. *Chem. - Eur. J.* **2016**, *22*, 18227. (i) Hu, Y.; Wang, X.-Y.; Peng, P.-X.; Wang, X.-C.; Cao, X.-Y.; Feng, X.; Müllen, K.; Narita, A. *Angew. Chem., Int. Ed.* **2017**, *56*, 3374. (j) Hosokawa, T.; Takahashi, Y.; Matsushima, T.; Watanabe, S.; Kikkawa, S.; Azumaya, I.; Tsurusaki, A.; Kamikawa, K. *J. Am. Chem. Soc.* **2017**, DOI: 10.1021/jacs.7b07113.
- (12) Bell, T. W.; Jousselin, H. *J. Am. Chem. Soc.* **1991**, *113*, 6283.
- (13) (a) Han, S.; Bond, A. D.; Disch, R. L.; Holmes, D.; Schulman, J. M.; Teat, S. J.; Vollhardt, K. P. C.; Whitener, G. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3223. (b) Han, S.; Anderson, D. R.; Bond, A. D.; Chu, H. V.; Disch, R. L.; Holmes, D.; Schulman, J. M.; Teat, S. J.; Vollhardt, K. P. C.; Whitener, G. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 3227.
- (14) (a) Flammang-Barbieux, M.; Nasielski, J.; Martin, R. H. *Tetrahedron Lett.* **1967**, *8*, 743. (b) Mallory, F. B.; Mallory, C. W. *Organic Reactions*; John Wiley & Sons, Inc.: Hoboken, NJ, 1984; Vol. 30, pp 1–456.
- (15) Liu, L.; Katz, T. J. *Tetrahedron Lett.* **1990**, *31*, 3983.
- (16) (a) Teplý, F.; Stará, I. G.; Starý, I.; Kollárovic, A.; Šaman, D.; Rulišek, L.; Fiedler, P. *J. Am. Chem. Soc.* **2002**, *124*, 9175. (b) Šamal, M.; Chercheja, S.; Rybáček, J.; Vacek Chocholoušová, J.; Vacek, J.; Bednářová, L.; Šaman, D.; Stará, I. G.; Starý, I. *J. Am. Chem. Soc.* **2015**, *137*, 8469. (c) Tanaka, K. In *Transition-Metal-Mediated Aromatic Ring Construction*; Tanaka, K., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2013; pp 281–298.
- (17) Kiel, G. R.; Ziegler, M. S.; Tilley, T. D. *Angew. Chem., Int. Ed.* **2017**, *56*, 4839.
- (18) (a) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788. (b) Yan, X.; Xi, C. *Acc. Chem. Res.* **2015**, *48*, 935. (c) Takahashi, T.; Xi, Z.; Yamazaki, A.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1998**, *120*, 1672. (d) Takahashi, T.; Hara, R.; Nishihara, Y.; Kotora, M. *J. Am. Chem. Soc.* **1996**, *118*, 5154.
- (19) While the fully intramolecular [2+2+2] cycloaddition of triynes (i.e., “cycloisomerization”) is heavily developed for helicene synthesis (refs 13 and 16), there have been very few applications of the partially intermolecular [2+2+2] cycloaddition of a diyne and monoyne. The latter is potentially more general, but it is also more difficult to control. For a notable example of a helicene-like compound produced in this way, see: Sawada, Y.; Furumi, S.; Takai, A.; Takeuchi, M.; Noguchi, K.; Tanaka, K. *J. Am. Chem. Soc.* **2012**, *134*, 4080.
- (20) Shirai, Y.; Osgood, A. J.; Zhao, Y.; Yao, Y.; Saudan, L.; Yang, H.; Yu-Hung, C.; Alemany, L. B.; Sasaki, T.; Morin, J.-F.; Guerrero, J. M.; Kelly, K. F.; Tour, J. M. *J. Am. Chem. Soc.* **2006**, *128*, 4854.
- (21) Paruch, K.; Katz, T. J.; Incarvito, C.; Lam, K.-C.; Rhatigan, B.; Rheingold, A. L. *J. Org. Chem.* **2000**, *65*, 7602.
- (22) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874.
- (23) Kezuka, S.; Tanaka, S.; Ohe, T.; Nakaya, Y.; Takeuchi, R. *J. Org. Chem.* **2006**, *71*, 543.
- (24) (a) Wu, J.; Fechtenkötter, A.; Gauss, J.; Watson, M. D.; Kastler, M.; Fechtenkötter, C.; Wagner, M.; Müllen, K. *J. Am. Chem. Soc.* **2004**, *126*, 11311. (b) Shao, C.; Grüne, M.; Stolte, M.; Würthner, F. *Chem. - Eur. J.* **2012**, *18*, 13665.
- (25) All pitches were calculated as described in the following: Enkhbayar, P.; Damdinsuren, S.; Osaki, M.; Matsushima, N. *Comput. Biol. Chem.* **2008**, *32*, 307.
- (26) Beurskens, P. T.; Beurskens, G.; van den Hark, T. E. M. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1976**, *5*, 241.
- (27) Martin, R. H.; Marchant, M. J. *Tetrahedron* **1974**, *30*, 347.